



**INTERNATIONAL EXPERTS WORKSHOP ON THE:  
"PRESENCE OF HEXAVALENT CHROMIUM IN DRINKING  
WATER"**

**January 15, 2011**

**ΣΥΝΑΝΤΗΣΗ ΔΙΕΘΝΩΝ ΕΜΠΕΙΡΟΓΝΩΜΟΝΩΝ ΓΙΑ ΤΗΝ «ΠΑΡΟΥΣΙΑ  
ΕΞΑΣΘΕΝΟΥΣ ΧΡΩΜΙΟΥ ΣΤΟ ΠΟΣΙΜΟ ΝΕΡΟ»**

**15 Ιανουαρίου 2011**

***The Greek Ministry of Environment, Energy and Climate Change in collaboration with the Greek Ministry of Health in order to provide updated answers to the problem of Hexavalent Chromium in drinking water is organizing the event***

**INTERNATIONAL EXPERTS WORKSHOP ON THE:  
"PRESENCE OF HEXAVALENT CHROMIUM IN DRINKING WATER"**

***to bring together leading international experts and top administrators from the European Union and the United States that will***

- ***Present the most recent scientific evidence***
- ***Share the regulatory experiences from the United States and the European Union***
- ***and Discuss with the Greek authorities and scientists the issues related to the presence of Cr(VI) in drinking water***

## SCHEDULE OF EVENT

FRIDAY, JANUARY 14, 2011

**AIR TRAVEL:** Flying into Greece.

**RECEPTION DINNER:** Casual get together for Experts to know each other and Ministry officials.

SATURDAY, JANUARY 15, 2011

THEME: GREETINGS AND INTRODUCTION

9 am-9:10 am: GREETING: MINISTRY OF ENVIRONMENT, ENERGY, AND CLIMATE CHANGE

9:10 am-9:20 am: GREETING: MINISTRY OF HEALTH AND SOCIAL SOLIDARITY

9:20-9:40 am: Dr. Andreas ANDREADAKIS: *Introduction to the Topic*  
SPECIAL SECRETARY FOR WATER  
GREEK MINISTRY OF ENVIRONMENT, ENERGY, & CLIMATE CHANGE  
PROF. NATIONAL TECHNICAL UNIVERSITY OF ATHENS

MORNING SESSION: SCIENTIFIC & REGULATORY CHALLENGES, NEEDS

9:40 am – 10:00 am: Dr. Alan T. STONE: *"Chemistry of Cr(VI) and its Transformation Products in Environmental Aqueous Media"*  
PROFESSOR (ENVIRONMENTAL AND AQUATIC CHEMISTRY)  
Department of Geography and Environmental Engineering  
G.W.C. Whiting School of Engineering  
JOHNS HOPKINS UNIVERSITY, MARYLAND

10:00 am -10:20 am: Dr. John A. IZBICKI: *Natural versus Anthropogenic Sources of Cr(VI), and methods to distinguish them*  
UNITED STATES GEOLOGICAL SURVEY (USGS)  
SAN DIEGO, CALIFORNIA

10:20 am– 10:40 am: Dr. Mitchell D. COHEN: *Toxicological Effects of Cr(VI) and Mechanisms of Chromium Uptake in the Body*  
ASSOCIATE PROFESSOR OF ENVIRONMENTAL MEDICINE  
NEW YORK UNIVERSITY LANGONE MEDICAL CENTER

COFFEE BREAK: 10:40 am – 10:55 am

10:55 am -11:15 am: Dr. Vassiliki KARAOULI:  
DIRECTOR "SANITARY ENGINEERING & ENVIRONMENTAL HYGIENE"  
GREEK MINISTRY OF HEALTH AND SOCIAL SOLIDARITY

11:15-11:35 am: **Dr. Nathalie ARNICH** *“Dietary Exposure of the French Population to Chromium and Review of the Toxicological data for Cr(III) and Cr(VI)”*

ANSES - THE FRENCH AGENCY FOR FOOD, ENVIRONMENTAL  
AND OCCUPATIONAL HEALTH SAFETY  
DIRECTION DE L’EVALUATION DES RISQUES (DER)  
UNITE D’EVALUATION DES RISQUES PHYSICO-CHIMIQUES (UERPC)

11:35 am-11:55 am: **Dr. Athena LINOS** *“Findings and Update of the Oinofyta Observatory Epidemiological Study”*

PROFESSOR OF EPIDEMIOLOGY & PREVENTION OF  
ENVIRONMENTAL OCCUPATIONAL DISEASES  
MEDICAL SCHOOL  
NATIONAL KAPODISTRIAN UNIVERSITY OF ATHENS

11:55 am-12:15 pm: **Dr. Dimitrios TRICHOPOULOS** *Epidemiological Studies of Effects of Cr(VI) with Emphasis on Oral Exposure*

VINCENT L. GREGORY PROFESSOR OF CANCER PREVENTION  
DEPARTMENT OF EPIDEMIOLOGY  
HARVARD UNIVERSITY, BOSTON

12:15 pm-12:35 pm: **Speaker**

12:35 pm- 12:55 pm: **Dr. George ALEXEEFF** *The California Experience: Public Health Goal for Cr(VI) in Drinking Water*

DEPUTY DIRECTOR FOR SCIENTIFIC AFFAIRS  
OFFICE OF ENVIRONMENTAL HEALTH HAZARD ASSESSMENT  
CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY (EPA)

**LUNCH BREAK: 12:55 pm to 14:30 pm**

**AFTERNOON SESSION: SCIENTIFIC & REGULATORY CHALLENGES, NEEDS**

14:30 pm – 14:50 pm: **Dr. Christopher PORTIER** *Policy and Regulatory Initiatives at the US Department of Health and Human Services Regarding Cr(VI)*

DIRECTOR NATIONAL CENTER FOR ENVIRONMENTAL  
HEALTH/AGENCY FOR TOXIC SUBSTANCES AND DISEASE  
REGISTRY (ATSDR)  
U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

14:50 pm – 15:10 pm: **Dr. Kurt STRAIF**

ACTING HEAD IARC MONOGRAPHS  
INTERNATIONAL AGENCY FOR RESEARCH ON CANCER  
WORLD HEALTH ORGANISATION

15:10 pm-15:30 pm: **Dr. Ir. Adriana D. HULSMANN**

KWR WATERCYCLE RESEARCH INSTITUTE  
DRINKING WATER/EU POLICY LEGISLATION

15:30 pm-15:50 pm: **Dr. Jan CORTVRIEN** *Closing Remarks and the EU Directive on*

*Quality of Water for Human Consumption*

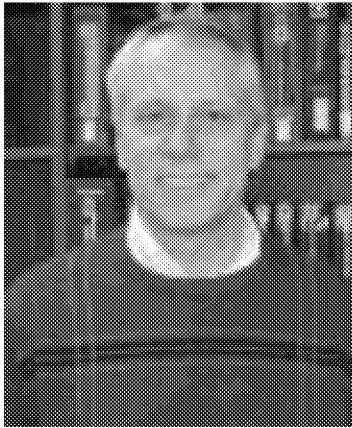
MARINE UNIT - DG ENVIRONMENT  
EUROPEAN COMMISSION

16:00 pm–17:30 pm: **ROUND TABLE DISCUSSION OF EXPERTS**

**RECEPTION DINNER**

LIST OF SPEAKERS  
SHORT BIOGRAPHICAL SKETCHES  
(Alphabetical Order)

Dr. George ALEXEEFF, Ph.D.



Deputy Director for Scientific Affairs  
Office of Environmental Health Hazard  
Assessment (OEHHA)

California Environmental Protection Agency  
(EPA)

#### Highlights of Dr. Alexeeff's Professional Career

Dr. Alexeeff is Deputy Director for Scientific Affairs, OEHHA, California EPA and also an Adjunct Professor in the Department of Environmental Toxicology at the University of California at Davis. He earned his Ph.D. in Pharmacology and Toxicology from the University of California at Davis and has been certified as a Diplomat of the American Board of Toxicology, Inc. (DABT) since 1986.

Dr. Alexeeff has reviewed over 140 documents evaluating human epidemiological or animal toxicological evidence for OEHHA or other agencies such as U.S. EPA.

He has recently served on the following National Academy of Sciences Committees: Review of the Federal Strategy to Address Environmental, Health, and Safety Research Needs for Engineered Nanoscale Materials (2008); Evaluating Efficiency of Research and Development Programs at the U.S. Environmental Protection Agency (2007); and Review the Office of Management and Budget Risk Assessment Bulletin (2006).

Dr. Alexeeff's professional activities include: President of the Northern California Chapter of the Society of Toxicology (2006-2007); President of the Genetic and Environmental Toxicology Association of Northern California (1995); member of the Society of Toxicology; charter member of the Society for Risk Analysis.

Dr. Nathalie ARNICH



ANSES

- French Agency for Food, Environmental and  
Occupational Health Safety –

Physico-Chemical Risk Assessment Unit

### Highlights of Dr. Arnich's Professional Career

Dr. Arnich is a Toxicologist Ph.D. with experimental experience on the bioavailability and toxicity of lead (Pb) in rats. In 2003 she joined AFSSA (the French Agency for Food Safety), at the Food Safety Directorate, Physico-Chemical Risk Assessment Unit. AFSSA became ANSES on July 1<sup>st</sup>, 2010 (the French Agency for Food, Environmental and Occupational Health Safety).

Dr. Arnich is in charge of the scientific coordination of the expert panel on Food Contact Materials (since 2009), and previously of the expert panel on Contaminants in food (2003-2009). She works in collaboration with the Drinking Water Unit and was involved in the latest French Total Diet Study regarding risk assessment associated with inorganic compounds (Pb, Cd, Hg, Al, As, Sb, Sn, Cr, Ni, Co).

She was also involved in the dietary risk assessment for biocide residues in food (European Review Programme under Directive 98/8/CE) and was member of 2 European working groups for the development of guidelines (2009-2010).

Her main contributions to AFSSA's assessments have dealt with:

- Bisphenol A
- Non dioxin-like polychlorinated biphenyls (NDL-PCBs)
- Polybrominated diphenyl ethers (PBDEs)
- Lipophilic marine biotoxins (*Dinophysis*, *Ostreopsis*)
- Chemical contaminants in shellfish
- Fipronil
- Health risks from non-compliance with drinking water parametric values.



Dr. Mitchell D. COHEN



Associate Professor  
Department of Environmental Medicine  
Editor-in-Chief, Journal of Immunotoxicology

New York University School of Medicine

### Highlights of Dr. Cohen's Professional Career

Dr. Cohen has held numerous elected offices in the Immunotoxicology Specialty Section (IMTOX SS) of the Society of Toxicology (SOT), including those of Vice President and President; he is currently also Chair of the IMTOX SS International Exchange Committee.

The editor of a **major text** in **Immunotoxicology** and an author/co-author of over 80 refereed journal publications Dr. Cohen has studied the effects of chromium since 1989; his works have been utilized as standard references among the major studies employed by the EPA, the US Department of Health, and other regulatory agencies for deriving safety standards for chromium agents.

Dr. Cohen's research interests include:

- Role of physicochemical properties in governing immunotoxic potentials of inhaled metals in the lungs.
- Effects of World Trade Center dusts on pulmonary biology/immunology related to the increased incidence of chronic lung disorders.
- The effect of inhaled pollutant gas/metal-induced changes in altered iron homeostasis (AIH) on macrophage functionality.
- Development of molecular methods to isolate/characterize DNA-protein cross-links, AND to assess mutagenicity/carcinogenicity of nickel, chromium, and vanadium agents.
- Determination of *in vitro* mechanisms of enzyme inhibition by metals.

## Dr. Adriana HULLSMANN



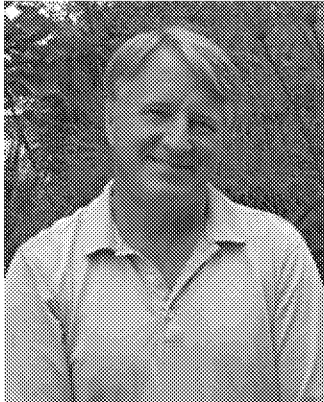
Dr. Ir. KWR Watercycle Research Institute

- Drinking Water and EU Legislation
- European Project Procurement and Project Management
- Management of European Water Cycle and Energy Network

### Highlights of Dr. Hulsmann's Professional Career

- Principal Scientific Officer at KWR Watercycle Research Institute, Netherlands: Drinking Water and EU Legislation.
- PREPARED Enabling Change FP7 February 2010-2014 Large Scale Integrated Project on the Adaptation of the water supply and sanitation sector to cope with climate change. DG Research EU.
- Decentralized Drinking Water Supply and Sanitation options. DGENV 2010.
- Assistance to the Bulgarian Government on the introduction of WISE (Water Information System for Europe) on drinking water quality data. Dutch Ministry of Economic Affairs. 2009-2010.
- DGENV consultant on the reporting obligations of EU Member States on the quality of drinking water; 1993-1995, 1006-1998, 1999-2001, 2002-2004 and 2005-2007 [last one in progress].
- Coordinator WSSTP Water Supply and Sanitation Technology Platform. DG Research. 2005-2006.
- Consultant at Estonia 2003 and Consultant at DG ENV 2005 (European Commission, Directorate General Environment). Organization of European Seminar on the Revision of the Drinking Water Directive 2003 DG ENV.
- WEKNOW Co-coordinator Web-based European Knowledge Network on Water, FP6 DG Research, concerted action, 2002-2005.
- Technical and Scientific Support European Commission Drinking Water Directives 80/778/EEC and 98/83/EC; Service contract obligations of Member States on the Standardized Reporting Directive 91/692/EC; European Commission DGENV: Processing, and analysis of data from Member States on water directives and production of synthesis reports; Participation in the Expert Advisory Forum on Reporting within the Framework Directive.
- Member of the Water Resources Panel, one of seven technical panels to ensure the Chartered Institution of Water and Environmental Management (CIWEM), UK fulfils its Royal Charter.
- Secretary, European Water Research Institutes (E.W.R.I.)
- Member, Experts Committee on Children's Environmental and Health Action Plan for Europe (CEHAPE).
  - Senior Scientist and Senior Adviser at Royal Haskoning, a 4,000-employee Dutch Engineering Company founded in 1881, with revenues over € 300million annually.

Dr. John A. IZBICKI



Research Hydrologist  
California Water Science Center

United States Geological Survey (USGS)

### Highlights of Dr. Izbicki's Professional Career

Dr. Izbicki has worked for the U.S. Geological Survey for 30 years and also is an Adjunct Professor at San Diego State University. His primary research interest is linking chemical, microbiological, and isotopic data to physical hydrologic processes. The past 20 years have been spent working on natural and artificial recharge processes in the Mojave Desert of California, understanding trace element occurrence in groundwater settings, evaluating seawater intrusion and brine invasion in coastal California aquifers, and identification of sources of fecal bacteria in coastal environments. Dr. Izbicki holds 2 patents for collection of coupled well-bore flow and depth-dependent water-quality data from wells.

Current projects include:

- Arsenic removal during artificial recharge through thick unsaturated zones
- Denitrification of septic discharges in thick unsaturated zones
- Chromium and chromium isotopic composition at contamination sites in the Mojave Desert
- Sources of fecal indicator bacteria near Malibu, California
- Use of chloride and oxygen isotopes to determine the source of natural and anthropogenic perchlorate, Rialto, California

Dr. Athena LINOS, MD, PhD, MPH



Professor of Epidemiology and Prevention of  
Environmental and Occupational Diseases  
Department of Hygiene, Epidemiology and  
Medical Statistics

Medical School

National and Kapodistrian University of Athens

### Highlights of Dr. Linos's Professional Career

Prof. Athena Linos studied Medicine at the University of Athens Medical School, and Public Health at Harvard School of Public Health, and trained at the Mayo Clinic Department of Epidemiology and Biostatistics for 3 years. She holds a PhD and Professorial degree from the University of Athens, Medical School in Epidemiology.

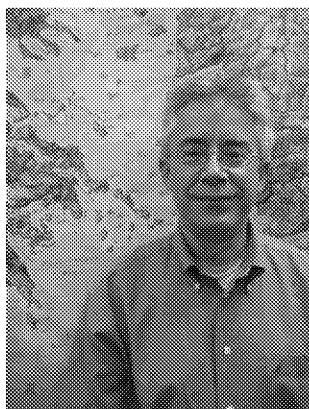
She has taught at the Mayo Medical School, the University of Minnesota, the Case Western Reserve University, and at the University of Athens (since 1982). She has been a visiting scientist/professor at the Mayo Medical School and the National Institutes of Health (NIH).

Prof. Linos activities include: Participation in Greek National Committees on public health and occupational health and safety; Vice President of the Greek Regulatory Agency for Medicines; President of the National Committee for Greek Diet; President of the Medicinal Products' Price Committee; President of the Institute of Preventive Medicine Environmental and Occupational Health, Prolepsis (since 1991).

Prof. Linos's work has focused on epidemiology and research methodology. She has researched chronic diseases (malignancies, rheumatoid arthritis, and endocrine disorders), and has worked in clinical research and pharmaco-epidemiology. She has participated in several environmental projects regarding cyclic hydrocarbons in seven European cities, the effect of water pipelines on public health, and the effect of pesticides on human health. She is currently the scientific coordinator of an observatory epidemiologic study in the Municipality of Oinofyta, Greece. Nutrition and obesity prevention have also been among her primary research interests.

Author and editor of many Greek and English textbooks on public health, Prof. Linos has also published extensively in international and Greek peer-reviewed journals, and has participated in numerous conferences. She is a member of several scientific associations and participates in many international networks for public health.

Dr. Allan T. STONE



Professor of Environmental and Aquatic  
Chemistry  
Department of Geography and Environmental  
Engineering  
G.W.C. Whiting School of Engineering  
  
Johns Hopkins University

### Highlights of Dr. Stone's Professional Career

Prof. Stone received his bachelor degree in Chemistry from the University of Maryland, College Park and Master's and Ph.D. degrees in Environmental Engineering Science from the California Institute of Technology.

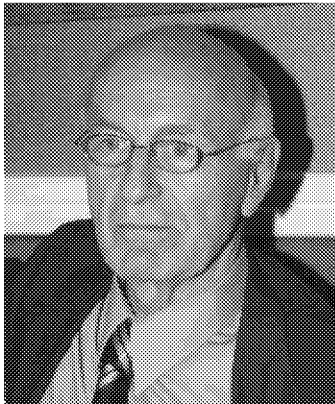
His research group at Johns Hopkins designs and conducts experiments that elucidate environmentally important transformation pathways. Metal ion-organic reactions, reactions at mineral surfaces, and the effects of chemical speciation are emphasized. His interests include:

- The properties and transformations of synthetic chemicals in environmental media.
- Natural biogeochemical processes, such as the acquisition of nutrients by plants, fungi, and bacteria and their role onto the geochemistry of soils.
- Inorganic species affecting water quality, e.g. disinfection by-product formation.
- The consequences of human activities regarding chemicals used in agriculture, forestry, aquaculture, and animal production on aquifers and other media, and the corresponding health effects and exposure.
- Appraising the consequences of past disposal practices, and devising management options.

Dr. Stone is the author of chapters related to topics on the fate of chemicals in the environment and their effect on ecosystem health, in over 12 books. He is the author of over 50 refereed journal publications.

Prof. Stone participates in activities that foster environmental chemistry education and research in other countries, e.g. the V Congreso Iberoamericano de Fisica y Quimica Ambiental, in Mar del Plata, Argentina. He has been a guest professor at the University of Karlsruhe, Germany.

Dr. Dimitrios TRICHOPOULOS, MD, PhD



Vincent L. Gregory Professor of Cancer  
Prevention  
and Professor of Epidemiology  
School of Public Health

Harvard University

### Highlights of Dr. Trichopoulos's Professional Career

Dimitrios Trichopoulos, MD, PhD has served as Professor and Chairman of the Department of Hygiene and Epidemiology, University of Athens Medical School; Chairman of the Department of Epidemiology, Harvard School of Public Health, and Director of the Harvard Center for Cancer Prevention. In addition to his current affiliation at Harvard University he is also Adjunct Professor of Medical Epidemiology at Karolinska Institutet, Sweden, and a Regular Member of the Athens Academy.

Distinctions include: Officier de l'Ordre des Palmes Académiques, France; Corresponding Member of the National Academy of Medicine (France) and the Royal Academy of Medicine (Belgium); Honorary Doctor of Medicine, University of Uppsala (1994); Smoke-Free America Award (1996); Commander of Honor of the Greek Republic (1996); Distinguished Physician, Hellenic Medical Society of New York (1999); Brinker International Award for Breast Cancer Research (2000); Julius Richmond Award for demonstrating the association of passive smoking with lung cancer (2004); Medal of Honour, International Agency for Research on Cancer - WHO (2007); Honorary Fellow, Royal College of Physicians, London, UK (2008).

Dimitrios Trichopoulos has authored or co-authored over 1000 publications, of which more than 700 are listed in international databases. He has done extensive work concerning breast cancer etiology, mainly focusing on the early life origins of this disease. He has published the original paper implicating passive smoking in the causation of lung cancer. He has contributed to the etiology of hepatocellular carcinoma, the quantification of the association between psychological stress and coronary heart disease and the identification of several dietary and other risk factors in the etiology of a number of cancers and other diseases.

## DOCUMENTS TO MOTIVATE DISCUSSION

(Kindly provided by the speakers)

## STATEMENT

UMWELTBUNDESAMT, ABTEILUNG TRINK- UND BADEBECKENWASSERHYGIENE  
(GERMAN FEDERAL ENVIRONMENT AGENCY  
DEPT. DRINKING-WATER AND SWIMMING POOL HYGIENE)  
CORRENSPLATZ 1  
14195 BERLIN  
GERMANY  
[www.umweltbundesamt.de](http://www.umweltbundesamt.de)

### TOXICOLOGICAL EVALUATION

The acute toxicity of Cr(VI) is relatively strong. A marker for high exposure to Cr(VI) and its peroxidative effect on lipids is the urinary excretion of malondialdehyde and possibly the activity of alpha-amylase, a digestive enzyme from pancreas, in blood serum.

A tolerable short term daily intake as based on health effects is 60 µg of Cr(VI) per kg body mass. It is based on adverse effects observed in the kidney and the gastrointestinal tract and on allergic reactions towards adducts from the reaction of proteins with the partially reduced Cr-species Cr(V) and Cr(IV).

Evaluation of the oral carcinogenic potential of genotoxic Cr(VI) at or after chronic exposure was and is controversial. However, Cr(VI) is reduced more or less completely to nontoxic Cr(III) during and after its uptake into the bloodstream. Therefore, at concentrations of Cr(VI) which might normally be expected in drinking water, "Chromium" possibly present there may be and is considered as not being genotoxic in vivo.

In Germany, in the early nineties we derived a life-long tolerable health limit for exposure of humans towards Cr(VI) of TDI = 5 µg/kg for all groups or subgroups of the general population. This TDI was extrapolated from a not yet nephro- and immunotoxic subchronic NOAEL of 2.4 mg/kg as observed in a Cr(VI) rat study and similarly from a subchronic gastrointestinal/hematologic LOAEL of 0.57 mg/kg for Cr(VI) in a case study with humans. From this TDI, we calculated a health based guide value for drinking water of 20 µg Cr(VI) per liter (rounded figure) if 10 % of the TDI would be allocated on 2 liter of drinking water per day and 70 kg-person.



Need to regulate Cr(VI) for its toxic potential?

This provisional drinking water guide value for Cr(VI) eventually was not implemented then in Germany for three reasons:

1) The concentrations of Cr(VI) in ground waters for drinking water production in Germany are low (95% of such ground waters contain less than a few  $\mu\text{g}$  Cr(VI) per liter, with maximal values around 5  $\mu\text{g/l}$ ).

2) The toxicological irrelevance (at the state of knowledge at the beginning of the nineties) of such very low Cr(VI) concentrations.

3) The impossibility at that time to routinely discriminate analytically at such low concentrations of Cr(VI), between Cr(III) and Cr(VI) - even in drinking water Cr(VI) exhibits a carcinogenic potential in vivo after inhalation. Recently, such potential was shown in vivo also after oral uptake by rats and mice at about 3 mg Cr(VI) per kg body mass and more with drinking water in a dose-dependent manner (Stout MD

<<http://www.ncbi.nlm.nih.gov/pubmed?term=%22Stout%20MD%22%5BAuthor%5D>>, Herbert RA

<<http://www.ncbi.nlm.nih.gov/pubmed?term=%22Herbert%20RA%22%5BAuthor%5D>>, Kissling GE

<<http://www.ncbi.nlm.nih.gov/pubmed?term=%22Kissling%20GE%22%5BAuthor%5D>>, Collins BJ

<<http://www.ncbi.nlm.nih.gov/pubmed?term=%22Collins%20BJ%22%5BAuthor%5D>>, Travlos GS

<<http://www.ncbi.nlm.nih.gov/pubmed?term=%22Travlos%20GS%22%5BAuthor%5D>>, Witt KL

<<http://www.ncbi.nlm.nih.gov/pubmed?term=%22Witt%20KL%22%5BAuthor%5D>>, Melnick RL

<<http://www.ncbi.nlm.nih.gov/pubmed?term=%22Melnick%20RL%22%5BAuthor%5D>>, Abdo KM

<<http://www.ncbi.nlm.nih.gov/pubmed?term=%22Abdo%20KM%22%5BAuthor%5D>>, Malarkey DE

<<http://www.ncbi.nlm.nih.gov/pubmed?term=%22Malarkey%20DE%22%5BAuthor%5D>>, Hooth MJ

Hooth MJ

<[http://www.ncbi.nlm.nih.gov/pubmed?term=%22Hooth%20MJ%22%5BAuthor%5D\(2009\) Hexavalent chromium is carcinogenic to F344/N rats and B6C3F1 mice after chronic oral exposure. Environ Health Perspect.](http://www.ncbi.nlm.nih.gov/pubmed?term=%22Hooth%20MJ%22%5BAuthor%5D(2009)%20Hexavalent%20chromium%20is%20carcinogenic%20to%20F344%20rats%20and%20B6C3F1%20mice%20after%20chronic%20oral%20exposure%20Environ%20Health%20Perspect.%20117(5):716-22)  
<javascript:AL\_get(this,%20'jour',%20'Environ%20Health%20Perspect.');>  
117(5):716-22).

## CONCLUSION

There is urgent need to characterize mechanistically and to quantify accordingly the oral carcinogenic potential of Cr(VI) and to falsify or verify any provisional Cr(VI) guide value as based up to now on non carcinogenic endpoints, including the guide value we derived provisionally in Germany in the early nineties (see above). This purpose would best be persecuted by an expert workshop (including experts from WHO drinking water guidelines) on evaluation and quantification of Cr(VI) effect mechanisms and modes of carcinogenic action at doses which correspond to the µg/l-range in drinking water.

## END STATEMENT

Communicated to us, and kindly provided us with permission to use it on November 17, 2010 by:

Dr. Birgit Mendel  
Bundesministerium für Gesundheit  
(German Federal Ministry of Health)  
Referat 324 "Trinkwasser"  
(Division 324 "Drinking Water")  
Rochusstr. 1  
D - 53123 Bonn  
Germany

# DRAFT

## Public Health Goal for Hexavalent Chromium in Drinking Water

Prepared by  
Pesticide and Environmental Toxicology Branch  
Office of Environmental Health Hazard Assessment  
California Environmental Protection Agency

August 2009

### DRAFT FOR PUBLIC COMMENT AND SCIENTIFIC REVIEW

### PUBLIC HEALTH GOAL FOR HEXAVALENT CHROMIUM IN DRINKING WATER

#### “SUMMARY

The Office of Environmental Health Hazard Assessment (OEHHA) is proposing a Public Health Goal (PHG) for hexavalent chromium of 0.06 parts per billion (ppb) or micrograms per liter ( $\mu\text{g/L}$ ) in drinking water. OEHHA has reviewed the available data on the toxicity of hexavalent chromium and has identified the proposed PHG level as protective against all identified toxic effects from both oral and inhalation exposure to hexavalent chromium that may be present in drinking water.

While hexavalent chromium has long been recognized as a potent carcinogen via inhalation, there is now sufficient concern that hexavalent chromium is also carcinogenic by the oral route of exposure, based on studies in rats and mice conducted by the National Toxicology Program (NTP, 2007b). To calculate the proposed PHG, OEHHA derived both an oral cancer slope factor of 0.6 (mg/kg-day)<sup>-1</sup>, based on a dose-related increase of tumors of the small intestine in male mice (NTP, 2007b), and an inhalation cancer slope factor of 510 (mg/kg-day)<sup>-1</sup>, based on occupational studies. OEHHA also used an exposure assessment (Keating and McKone, 1993) to estimate inhalation of waterborne hexavalent chromium during showering. The combined-route cancer risk is dominated by the oral exposure despite the much higher inhalation potency, because the inhalation of water droplets during showering is very small. The resulting proposed PHG is quite low, based on the linear extrapolation to a one in one million lifetime cancer risk from the high incidence of tumors observed in the mice.

A health-protective level of 2 ppb for non-carcinogenic effects is also proposed based on liver toxicity (mild chronic inflammation, fatty changes) in female rats in the NTP

study (2007b). Other studies have indicated adverse effects in the liver and blood forming tissues.

Chromium is a heavy metal that occurs throughout the environment. The soluble hexavalent form is relatively toxic, while the less-soluble trivalent form has very low toxicity and is a required nutrient. The two forms are inter-convertible in the environment.

Available studies characterized the carcinogenic and non-carcinogenic activity of hexavalent chromium resulting from inhalation or oral exposure in both experimental animals and humans. Most of the toxicity studies investigated carcinogenic activity, because hexavalent chromium has been identified as a carcinogen. Other studies focused on the pharmacokinetics of hexavalent and trivalent chromium. The findings of these studies are very important in understanding the toxic actions of this metal.

Following oral administration of hexavalent chromium to humans and experimental animals, increased levels of chromium in whole blood and plasma were observed, while little change was observed following trivalent chromium administration. Increases in blood/plasma chromium levels following oral hexavalent chromium administration demonstrate bioavailability of the hexavalent form of the metal. Demonstrating bioavailability for orally administered products through increases in plasma and/blood levels is a routine method (required, for example, in submitting new drug applications).

It has been suggested that hexavalent chromium is completely converted to trivalent chromium in the acidic environment of the stomach, and therefore poses a negligible risk of toxicity (carcinogenic or non-carcinogenic) by the oral route (De Flora *et al.* 1997; Proctor *et al.*, 2002b). Complete conversion of hexavalent chromium to trivalent chromium in the stomach would result in the two forms behaving identically with respect to absorption, distribution, and toxic effects. However, as mentioned above, differences in blood/plasma levels have been observed. In addition, studies in animals and humans have revealed that orally administered hexavalent chromium results in elevated chromium tissue levels and increased urinary half-life compared to administered trivalent chromium. Increased toxicity following oral exposure to hexavalent chromium (compared to trivalent chromium) also suggests that hexavalent chromium is not completely converted to trivalent chromium in the stomach. After absorption into the body, the hexavalent form is eventually reduced to the trivalent form.

Given the abundant evidence that indicates hexavalent chromium is not completely converted to trivalent chromium in the stomach and that a fraction of orally administered hexavalent chromium is bioavailable, the evidence of potential carcinogenic and non- carcinogenic effects of the hexavalent form of the metal needed to be evaluated.

Evidence on carcinogenic effects of hexavalent chromium has been summarized by others, principally for the inhalation route (IARC, 1990). Evaluation of carcinogenic risk for this assessment focused on the evidence of systemic availability and the

resulting risk of carcinogenic effects after oral exposure. Studies of the mechanism of action of hexavalent chromium suggest a carcinogenic response if hexavalent chromium enters cells, regardless of the route of exposure. Orally administered hexavalent chromium results in genotoxicity at sites distal to the site of entry, the gut, which indicates that chromium reaches those sites in the hexavalent form. Administration via drinking water of hexavalent chromium to mice (Borneff *et al.*, 1968) resulted in a statistically significant increase in stomach tumors compared to controls (OEHHA analysis). Administration of hexavalent chromium in drinking water to male and female F344 rats resulted in a statistically significant increase in papillomas or carcinomas of the oral cavity in the high dose group (NTP, 2007b). Administration of hexavalent chromium in drinking water to male and female B6C3F1 mice resulted in a statistically significant and dose-related increase in adenomas or carcinomas of the small intestine (NTP 2007b).

Exposure of a human population to hexavalent chromium in drinking water resulted in a statistically significant increase in stomach tumors compared to rates in the surrounding province (Zhang and Li, 1987). Review of occupational studies in which humans were exposed to hexavalent chromium primarily by the inhalation route revealed an increase in stomach cancer, which suggests that cells in the stomach are being exposed to hexavalent chromium, although the primary exposure route was inhalation. An examination of this evidence provides further support to consider hexavalent chromium to be carcinogenic by the oral exposure route.

The existing California and U.S. Environmental Protection Agency (U.S. EPA) Maximum Contaminant Levels (MCLs) of (total) chromium in drinking water are 50 ppb and 100 ppb (50 µg/L and 100 µg/L), respectively. Neither of these regulatory levels are specific for hexavalent chromium, and neither involves the assumption of potential carcinogenicity of hexavalent chromium. The California Detection Limit for the Purposes of Reporting, or DLR, is 10 ppb for total chromium in drinking water. Hexavalent chromium was detected in 1,997 out of over 6,400 water sources analyzed as of April 6, 2004 (CDHS, 2004), with a DLR of 1 ppb. About 10 percent of the samples had reported levels of 5 ppb or more.

The proposed PHG is intended to help guide the California Department of Public Health in developing a Maximum Contaminant Level for hexavalent chromium in drinking water, as defined in the Safe Drinking Water Act. PHGs are not developed as target levels for cleanup of contamination of ground or ambient surface water or other environmental media, and may not be applicable for such purposes, given the regulatory mandates and constraints of other environmental programs.”

**END SUMMARY OF THE 142 PAGE DRAFT FOR PUBLIC COMMENT AND SCIENTIFIC  
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*U.S. public document, e-mail on 18-11-2010, Dr. George Alexeeff, Deputy Director for Scientific Affairs, California EPA.*